CLAIMS

1. Use of divalent or trivalent metallic cations to improve the functional activity of antibodies.

2. Use of claim 1, characterized in that said antibodies are human IgGs or having a human Fc region.

3. Use of claim 1 or 2, characterized in that said cations interact with the Fc region of said antibodies.

4. Use of anyone of claims 1 to 3, characterized in that said cations take part in controlling the opening of the Fc region of said antibodies.

5. Use of anyone of claims 1 to 4, characterized in that said cations promote fixing of said antibodies to the FcγR receptors, in particular the FcγRIII receptor.

6. Use of anyone of claims 1 to 5, characterized in that said cation is zinc, iron, copper or cadmium.

7. Use of anyone of claims 1 to 6, characterized in that said cation is zinc.

8. Method for potentialising the functional activity of antibodies via the Fc region, comprising a step consisting of adding a suitable quantity of at least one divalent or trivalent metallic cation to the biological system producing the antibodies or to a solution comprising antibodies before and/or after purification, or to the storage solution, or to the end formulation in the form of an injectable solution of antibodies.

9. Method of claim 8, characterized in that said cation is zinc, iron, copper or cadmium.

10. Method of claim 9, characterized in that a zinc molar concentration is added at least equal to the molar concentration of antibody.

11. Class IgG3 antibody having a fixing site for a divalent or trivalent metallic cation comprising the His 310 and His 435 residues (Kabat numbering) on its Fc site created by molecular engineering.

12. Antibody of claim 11, characterized in that said fixing site comprises the Asn 434 residue and/or the His 433 residue (Kabat numbering).

13. Antibody of claim 11 or 12, characterized in that said fixing site is created by substitution of Arg 435 by His 435.

14. Antibody of claim 11 or 12, characterized in that at least one of said histidine residues is replaced by at least one of the residues chosen from among cystein, aspartic acid and glutamic acid.

15. Antibody of anyone of claims 11 to 14, characterized in that it has a divalent or trivalent metallic cation fixed onto said fixing site.

16. Antibody of anyone of claims 11 to 15, characterized in that said cation is zinc, iron, copper or cadmium.

17. Antibody of anyone of claims 11 to 16, characterized in that the allotype of said antibody is G3m(b) or G3m(g).

18. Antibody of anyone of claims 11 to 17, characterized in that it has improved fixing to FcγRIII and improved functional activity with respect to the native antibody.

19. Use of the antibody of anyone of claims 11 to 18, for the preparation of a medicinal product to treat pathologies such as haemolytic disease of the newborn, a viral, bacterial or parasitic pathology, a pathology related to pathogenic agents or derived toxins, listed as being particularly dangerous in the event of bioterrorism (classification of the Centers for Disease Control, CDC), in particular anthrax (Bacillus anthracis), botulism (Clostridium botulium), the plague (Yersinia pestis), smallpox (Variola major), tularaemia (Francisella tularensis), viral haemorrhagic fevers (related to filoviruses: Ebola, Marburg and to arenaviruses - Lassa, Machupo), the epsilon toxin of Clostridium perfringens, brucellosis (Brucella species), melioidosis (Burkholderia mallei) the toxin of castorbean (Ricinus communis).

20. Pharmaceutical composition of therapeutic antibodies comprising divalent or trivalent cations and at least one excipient.

21. Composition of claim 20, characterized in that said antibodies have a divalent or trivalent metallic cation on the His 310 and His 435 residues (Kabat numbering).

22. Pharmaceutical composition of claim 20 or 21, characterized in that said antibodies are the antibodies of claims 11 to 18 or human IgGs or having a human Fc region.

23. Pharmaceutical composition of anyone of claims 20 to 22, characterized in that the metallic cations are zinc, iron, copper or cadmium, or a mixture of several of these.

24. Pharmaceutical composition of claim 23, characterized in that said cation is zinc, in particular zinc acetate, zinc bromide, zinc citrate, zinc hydroxycarbonate, zinc iodide, zinc L-lactate, zinc nitrate, zinc stearate, zinc gluconate, zinc sulphate, zinc chloride or zinc hydrochloride.

25. Pharmaceutical composition in which at least 50%, 60%, 70%, 80%, 90% or even 99% of the antibodies have a bound divalent or trivalent metallic cation, in particular bound to the site comprising the His 310 and His 435 residues (Kabat numbering).

26. Composition of claim 25, characterized in that said site comprises the His 433 and/or Asn 434 residues (Kabat numbering).

27. Composition of claim 25 or 26, characterized in that said metallic cation is zinc, iron, copper or cadmium or a mixture of several of these.

28. Solution comprising a monoclonal antibody or polyclonal antibodies and a suitable quantity of divalent or trivalent metallic cation, in particular a zinc ion concentration at least equal to the antibody concentration, said solution being adapted for injection via intravenous, intramuscular or subcutaneous route.

29. Use of zinc ions to improve the crystallisation of therapeutic antibodies.

30. Test which can be used to assess the efficacy of an antibody, comprising study of the 3D conformation of the domain involving His 310, His 435, His 433 and/or Asn 434 (Kabat numbering) such as shown in figure 1 or 2, or an assay of the zinc content of said antibodies, the presence of zinc being an indication of the efficacy of the antibody.

31. Antibody having modification of at least one of its His 310 and His 435 residues (Kabat numbering).

32. Antibody of claim 31, characterized in that said modification is a mutation.

33. Antibody of claim 32, characterized in that said mutation is a substitution by an amino acid having a low affinity for said metallic cations.

34. Antibody of claim 33, characterized in that said amino acid is lysine, alanine, glycine, valine, leucine, isoleucine, proline, methionine, tryptophan, phenylalanine, serine or threonine.

35. Antibody of anyone of claims 32 to 34, characterized in that the His 310 and His 435 residues are substituted by lysine residues.

36. Antibody of claim 31, characterized in that the modification is made by DEPC.

37. Antibodies of anyone of claims 31 to 36, characterized in that they belong to the IgG1 sub-class.

38. Antibodies of anyone of claims 31 to 37, characterized in that they have reduced functional activity with respect to the same non-modified antibody.

39. Use of anyone of antibodies 31 to 38 to prepare a medicinal product intended to prevent graft rejection or for the treatment of a pathology chosen from among tetanus, diphtheria, or caused by a pathogenic agent or derived toxin, listed as being particularly dangerous in the event of bioterrorism (classification of the Centers for Disease Control, CDC), in particular anthrax (Bacillus anthracis), botulism (Clostridium botulium), the plague (Yersinia pestis), smallpox (Variola major), tularaemia (Francisella tularensis), viral haemorrhagic fevers (related to filoviruses: Ebola, Marburg and to arenaviruses - Lassa, Machupo), the epsilon toxin of Clostridium perfringens, brucellosis (Brucella

species), melioidosis (Burkholderia mallei) the toxin of castorbean (Ricinus communis).

40. Use of the antibody of anyone of claims 31 to 38 for the preparation of a medicinal product to replace IgG4s.